

REMARKS

Formal Matters

In the specification, the paragraph at page 3, lines 33-34 (*i.e.*, description of Figures 2A and 2B) has been amended to recite that SEQ ID NO:1 is the sequence identification number of the human *ptch* nucleic acid.

Claim Objections

Claims 29, 30, 39, 40 and 49 have been amended to correct the observed informalities.

Claims 29-54 remain in this application. No claim has been canceled or added. Claims 29-33, 39-43 and 49 are amended. No new matter is added by the amendments. Support for the amendments is found throughout the specification, and specifically at least as indicated below:

Claims 31-33, 41-43, "at least one" and "one": page 11, lines 15-17.

Claims 29, 39, "1 to 5 conservatively substituted, added or deleted": page 11, lines 22-27.

Claims 29, 39, 49, "specifically binds": page 49, lines 7-8.

Claims 29 and 39, "hedgehog polypeptide: page 49, Example 6.

In view of the Examiner's earlier restriction requirement, Applicants retain the right to present withdrawn and cancelled subject matter in subsequent prosecution.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 29, 31-39 and 41-48 are rejected under 35 U.S.C. § 112, first paragraph - enablement, allegedly because while the specification, while enabling for an antibody that binds SEQ ID NO:2, is not enabling for any antibody that binds to a variant of SEQ ID NO:2.

Specifically, the Examiner alleges that Applicants have disclosed only a single working example of a patched-2 polypeptide with greater than 91% sequence identity to SEQ ID NO:2 and which binds to a hedgehog or Smoothened polypeptide. The Examiner continues with a recitation of the 8 Wands factors, further alleges that the specification does not provide any

specific guidance as to which amino acid residues could be modified so as to produce a polypeptide that is not identical, yet still retains the activity of the native sequence polypeptide. Moreover, the Examiner alleges that there is no guidance as to the nature and extent of changes that can be made at these positions. The Examiner further alleges that Applicants have not defined a difference in structure, or difference in function, between the protein corresponding to the patched-2 native sequence and its variants.

In response, Applicants have amended the claims to define a patched-2 variant as a polypeptide that has from 1-5 conservatively substituted, deleted or added amino acid residue and which binds to hedgehog. Thus, Applicants have now defined patched-2 variants in a manner which precisely identifies the extent and nature of the structural changes in addition to the overall functional requirement.

Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 29, 31-39 and 41-48 under 35 U.S.C. § 112, First Paragraph.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 29, 31-39 and 41-48 are rejected under 35 U.S.C. § 112, first paragraph - written description because, allegedly because while the specification indicates Applicants' possession of SEQ ID NO:2, the specification fails to disclose any other patched-2 variant protein that can bind hedgehog or smoothened.

Specifically, the Examiner alleges that the specification fails to provide definitive structural or functional features, or critical conserved regions of the genus of patched-2 polypeptides that retain binding to hedgehog or smoothened.

In response, Applicants respectfully submit that Applicants' previous arguments addressing the enablement rejection of the same claims are also responsive to this written description rejection. Additionally, Applicants respectfully submit that the definition of variant as being from 1 to 5 conservatively substituted, added or deleted amino acid residues of SEQ ID

NO:2 specifically and particularly identifies the nature and structural characteristics (and therefore possession) of the variant polypeptides.

Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 29, 31-39 and 41-48 under 35 U.S.C. § 112, First Paragraph.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 29-48 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention.

Specifically, the Examiner asserts that Claims 29 and 39 are indefinite because it is unclear if "Smoothened" refers to nucleic acid or polypeptide.

In response, Applicants have adopted the Examiner's recommendation.

Rejection Under 35 U.S.C. § 103(a) (cited references)

Claims 29-33, 35-43, 45-49 and 51-54 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Motoyama *et al.*, *Nat. Genet.* 18(2): 104-6 in view of Tso *et al.*, U.S.P. 5,932,488.

Claims 29, 34, 39, 44, 49 and 50 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Motoyama *et al.*, *Nat. Genet.* 18(2): 104-6 in view of Liddell *et al.*, *Antibody Technology*, BIOS Scientific Publishers, 1995, pages 9-24 and 85-102.

Specifically, the Examiner alleges that Motoyama *et al.* discloses a mouse polypeptide that is 89.3% similar to SEQ ID NO:2, while Tso *et al.*, U.S.P. 5,932,488 allegedly describes monoclonal, bispecific and heteroconjugated antibodies, while Liddell is alleged to disclose polyclonal antibodies.

The Examiner alleges that due to the high degree of similarity to the Motoyama sequence and SEQ ID NO:2, including numerous regions of 20 or more amino acids with 100% sequence

identity, that it would be obvious that antibodies that bind to the murine Motoyama sequence would also bind the human SEQ ID NO:2 sequence.

In response, Applicants have amended Claim 29, 39 and 49 to specifically state that the antibodies specifically bind SEQ ID NO:2. The hypothetical antibodies asserted in the Examiner's arguments would not be specific to SEQ ID NO:2.

Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 29-33, 35-43, 45-49 and 51-54 under 35 U.S.C. § 103(a).

SUMMARY

Claims 29-54 are pending in the application.

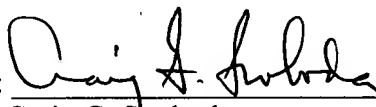
If in the opinion of the Examiner, a **telephone conference** would expedite the prosecution of the subject application, the Examiner is **strongly encouraged** to call the undersigned at the number indicated below.

This response/amendment is submitted with a transmittal letter and petition for a 3-month extension of time and fees. In the unlikely event that this document is separated from the transmittal letter or if fees are required, applicants petition the Commissioner to authorize charging our Deposit Account 07-0630 for any fees required or credits due and any extensions of time necessary to maintain the pendency of this application.

Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Respectfully submitted,
GENENTECH, INC.

Date: **January 10, 2006**

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